REMARKS

I. Status of the claims

Claims 1-23, 28, 29, and 39-44 are pending in this application. Claims 3, 9, and 41-44 have been withdrawn by the Office for being directed to non-elected subject matter. No claim has been amended in this Response.

II. Rejections under 35 U.S.C. § 103

Claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent No. 4,946,870 ("*Partain*"), in view of the Encyclopedia of Controlled Drug Delivery, vol. 1, 2 (1999), and U.S. Patent No. 5,411,981 ("*Gaillard-Kelly*"). Claims 5, 6, 10, 14, 15, 18-21, 39, and 40 stand rejected as allegedly being unpatentable over *Partain*, *Gaillard-Kelly*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29, in further view of the respective references, as follows: U.S. Patent No. 5,916,910 ("*Lai*") (claim 14); US Patent No. 5,541,220 ("*Ismail*") (claim 15); EP 0427625 A (claims 18 and 19); WO 92/21317 (claims 18 and 20); WO 91/19701 (claims 18 and 21); Cremophor RH 40 Technical Information, 1997 ("Cremophor pamphlet") (claims 5 and 6); and US Patent No. 5,658,559 ("*Smith*") (claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40).

The Office remains unpersuaded by any of Applicants' arguments expressed in the previous Reply to Office Action, and has not introduced new reasons for rejecting the claims. Thus, Applicants maintain their traversal of the Office's rejection of the

Claims for the reasons of record, as well as for the following additional arguments in response to the Office's rationale for not accepting Applicants' prior arguments.

In particular, the Office continues to be unpersuaded by Applicants' argument that the cited art fails to teach the inclusion of a plasticizer in a composition, as provided by a limitation of independent claim 1, the claim from which all other claims depend. Specifically, the Office argues that *Partain* "teaches a glycerin-containing controlled-release formulation, which renders the use of glycerin an obvious choice [for a plasticizer]," citing *Partain* at Example 14, which discloses a composition that comprises glycerin. Office Action at 11.

The Office acknowledges that the *Partain* fails to explicitly provide teachings related to the inclusion of a plasticizer in a composition, by stating "*Partain* does not mention that a plasticizer is used in the composition, but glycerine, as used in Example 14, is a well-known plasticizer in controlled release pharmaceutical art." Office Action at 3. In order to cure the deficiency of *Partain* relating to the lack of teaching that the exemplified composition comprises a plasticizer, the Office relies on Table 1 of the "Encyclopedia of Controlled Drug Delivery," which discloses several compounds, including glycerin, that under certain circumstances have been used as plasticizers. Office Action at 3.

Foremost, Applicants point out that the Encyclopedia of Controlled Drug Delivery is not proper prior art against the rejected independent claims. The Encyclopedia of Controlled Drug Delivery was published in 1999, which is later than the benefit of priority accorded to this application by virtue of its two priority documents: DE19981048856 (filed October 23, 1998) and DE19991000749 (January 12, 1999).

The Supreme Court in the recent *KSR* decision mandates that "[t]o facilitate review, this analysis [of whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue] should be **made explicit**." *KSR Int'l Co. v. Teleflex Inc., et al.*, 127 S. Ct. 1727, 1741 (2007) (emphasis added) (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) ("[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.")).

The recent PTO Examination Guidelines to Determine Obviousness echo this requirement by indicating that "[t]he key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious." Examination Guidelines to Determine Obviousness under 35 U.S.C. § 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Fed. Reg. 72(195):57526-57535, 57528, col. 3 (Oct. 10, 2007) ("*Obviousness Guidelines*.")

A. Glycerin is not always a plasticizer

Thus, in view of the Office's own instructions regarding obviousness rejections, Applicants respectfully point out that the Office has failed to articulate any reason why one of ordinary skill in the art after reading *Partain*, or any other cited reference, would combine a ***plasticizer*** with the compounds of *Gaillard-Kelly*. The Office cites to the Encyclopedia of Controlled Drug Delivery to support its conclusion that "glycerin is a plasticizer according to the prior art." Office Action at 12. However, with respect to glycerin, the reference simply states that "[t]his multipurpose excipient *has been used*

as a plasticizer." Encyclopedia of Controlled Drug Delivery at 309. In other words, **the reference does not state that glycerin is a plasticizer**, but rather that it *has been* used as a plasticizer, *i.e.*, that under some circumstances glycerin could be used as a plasticizer. A substance that is a plasticizer in a particular formulation may not be a plasticizer in a different formulation. The reference explains that "[p]lasticizers must be compatible, in terms of solubility parameter, with the [controlled release] polymer to which they are added to make it more flexible. Importantly, **plasticizers are not general purpose compounds**, but must be chosen on the basis of their usefulness for a particular polymer." *Id.* at 307 (emphasis added). Accordingly, even if glycerin has been used as a plasticizer, glycerin **is not always a plasticizer**.

The Office has not shown that the combination of the cited references would result in a composition comprising at least one plasticizer

Applicants respectfully remind the Office that the rejected claims do not recite a composition comprising "glycerin," but rather a composition comprising "at least one plasticizer." *See*, *e.g.*, claim 1. Even assuming, *arguendo*, that the cited references would have suggested the use of glycerin in combination with the compounds of *Gaillard-Kelly*, glycerin is a multi-functional substance, and may be included in a composition for many purposes, including for example, to function as an emulsifier, or to make a formulation isotonic. *See*, *e.g.*, *Modern Pharmaceutics*, third edition, published by Marcel Dekker, Inc., New York, NY, 1996, at 461 and 460 (copies of relevant pages are enclosed for the office's convenience.) In addition, *Remington: The Science and Practice of Pharmacy*, 20th edition, published by Lippincott Williams & Wilkins, Baltimore, MD and Philadelphia, PA, 2000, states at page 1039 that: "[o]ne of the most

valuable products known to pharmacy [is glycerin] by virtue of its *solvent* property;" and that "[i]t is useful as a *humectant* in keeping substances moist, owing to its hygroscopicity" (copies of relevant pages are enclosed for the office's convenience.)

Applicants respectfully remind the Office that the Office "bears the initial burden of factually supporting any prima facie conclusion of obviousness." M.P.E.P. § 2142. Given the diverse uses of glycerin in pharmaceutical compositions, the skilled artisan could not have looked to Example 14 of *Partain* and axiomatically found teachings relating to a plasticizer. The Office has already acknowledged that *Partain* fails to teach a plasticizer. Thus, Applicants reiterate their longstanding argument that one of skill in the art at the time of the invention could not have looked to the *Partain* and *Gaillard-Kelly* disclosures and determined that a plasticizer should be included in the claimed composition, without knowledge of Applicants' invention. In this regard, Applicants again respectfully point out that obviousness should be viewed through the eyes and mind of one skilled in the art back in time at the moment the invention was made, and without the benefit of the applicant's disclosure. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). This approach is also advocated in the *Obviousness Guidelines*, which state that "the focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge." *Obviousness Guidelines*, Fed. Reg. 72(195) at 57527, col. 3.

Previously, Applicants argued that if one of ordinary skill in the art were to combine *Partain* with *Gaillard-Kelly* because both references teach anti-alopecia or

acne compositions, such artisan would naturally seek guidance in *Partain* regarding formulations useful for the treatment of alopecia or acne, yet none of these formulations comprises glycerin or a plasticizer. Instead, as acknowledged by the Office, the only composition comprising glycerin disclosed in *Partain* is Example 14, which refers to an *antihistamine* lotion. The Office asserts that "[a] reasonable skilled artisan would not have considered the illustration of using glycerine in an antihistamine lotion as an indication that the *only* application that glycerine is suitable is an antihistamine lotion." Office Action at 11. However, Applicants respond by emphasizing that, without teachings by the cited references that glycerin was included in an exemplified composition to function as a plasticizer, the skilled artisan could not have divined that a plasticizer should be a component of the claimed invention. Thus, Applicants submit that the issue is not whether or not glycerin was suitable only for use in an antihistamine lotion, as framed by the Office, but rather, whether the cited references suggest the use of a plasticizer as instantly claimed.

For the foregoing reasons, the rejected claims would not have obvious in light of the cited art. Accordingly, Applicants respectfully request that this rejection be withdrawn.

B. Claim 14

The Office rejected claim 14 under 35 U.S.C. 103(a) as allegedly being unpatentable over Gaillard-Kelly, Partain, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 above, and further in view of U.S. Patent No. 5,916,910 ("*Lai*"). As mentioned previously, the

Encyclopedia of Controlled Drug Delivery is not proper prior art to this claim. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Claim 14 recites *[a] composition as claimed in claim 11, wherein at least one angiotensin converting enzyme inhibitor is chosen from quinapril, lisinopril, benzazepril, captopril, ramipril, fosinopril, cifazapril, and tradolapril.* The Office acknowledges that the "combined references fail to teach angiotensin converting enzyme inhibitors." Office Action at 4. However, the Office argues that:

> Lai teaches conjugates of dithiocarbamates with pharmacologically active agents, wherein dithiocarbamates are said to reduce cutaneous irritation and alopecia. See col. 3, lines 49-51. Captopril, fosinopril, felopdipine, nicardipine, and nifedipine are taught as pharmaceutical agents that are added for modification. See col. 8, lines 51-54.

Office Action at 4-5.

The Office then argues that it would have been obvious to one of ordinary skill in the art "to have modified the teachings of the combined references by adding to the composition captopril as motivated by *Lai* because all the references are directed to treating alopecia, and Lai teaches captopril are [sic] combined with other anti-alopecia agents." Id. at 5. The Office also argues that the "Lai reference suggests that treatment for alopecia is needed for cancer patients, and a skilled artisan would certainly find the controlled release formulations for alopecia as taught by Partain/Encyclopedia/Gaillard-Kelly applicable in anticancer drugs." Office Action at 12. Applicants courteously disagree.

In response, Applicants respectfully point out that the Office has misinterpreted the teachings of *Lai*. *Lai* does not provide teachings of captopril being used in

combination with anti-alopecia agents. Instead, *Lai* teaches that alopecia, a side effect of the chemotherapeutic agent Adriamycin, can be reduced if Adriamycin is conjugated to a dithiocarbamate, because dithiocarbamate-conjugated Adriamycin is targeted more efficiently to cells. *Lai* at col. 3, lines 48-53. *Lai* merely lists captopril as one of many antihypertensive drugs that can be modified by conjugation to dithiocarbamates, and does not teach that captopril causes alopecia. *Lai* at col. 8, lines 44-64. However, the dithiocarbamate moiety of the dithiocarbamate-conjugated Adriamycin does not treat alopecia *per se*, it simply reduces the hair-loss effects of Adriamycin. Thus, Applicants submit that a skilled Artisan could not have looked to *Lai* to find teachings that associate captopril with hair loss or hair loss treatment, *per se*.

Lai also does not provide teachings of captopril being combined with Adriamycin or dithiocarbamate-Adriamycin conjugates. While *Lai* teaches that captopril, like Adriamycin, can be conjugated with dithiocarbamates, there is no teaching in *Lai* that captopril reduces alopecia or that it can be combined with anti-alopecia agents. *Lai* at col. 7, lines 41-52. Therefore, there is no support in *Lai* for the Office's statement that "Lai teaches captopril [is] combined with other anti-alopecia agents." Office Action at 5. Thus, because *Lai* is not directed to combining captopril with an anti-alopecia agent, and does not contain teachings of angiotensin converting enzyme inhibitors, Applicants submit that the Office has not identified any reason why one of ordinary skill in the art would have combined *Lai* with the teachings of *Partain* and *Gaillard-Kelly.* For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Additionally, claim 14 depends from claim 1, which as explained above, would not have been obvious in light of the cited references, at least because the combined

references fail to teach a composition comprising a plasticizer. *Lai* was cited only for its alleged disclosure of captopril in the treatment of alopecia and fails to cure the deficiencies of the rest of the cited references. Therefore, because claim 14 incorporates the subject matter of claim 1, and claim 1 is not obvious over the cited art, claim 14 cannot be obvious in light of the cited references either.

C. Claim 15

The Office rejected claim 15 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 above, and further in view of US Patent No. 5,541,220 ("*Ismail*"). Office Action at 5. As mentioned previously, the Encyclopedia of Controlled Drug Delivery is not proper prior art to this claim. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Claim 15 recites "[a] composition as claimed in claim 11, wherein at least one methylxanthine compound is chosen from pentoxifyllin, propentofyllin, and torbafyllin. The Office acknowledges that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach methylxanthine compounds. Office Action at 5. The Office argues, however, that *Ismail* teaches agents for the treatment or protection of the skin and that *Ismail* exemplifies "a capsule that can treat alopecia, comprises pentoxifylin, vitamin E, and other ingredients." *Id.* The Office argues that it would have been obvious to one of ordinary skill in the art to add pentoxifylin to the composition of the combined references because *Ismail* and the references are directed to treating alopecia and *Ismail* teaches pentoxifyiline as increasing blood circulation. The Office

further argues that the skilled artisan would have been motivated to add pentoxifyline to the composition of the combined references because of the expectation of circulating the active agents of the composition through the body.

Claim 15 depends from claim 1 and would not have been obvious in light of the cited references, at least because the combined references fail to teach a composition comprising a plasticizer. *Ismail* was cited only for its disclosure of pentoxifyline and fails to cure the deficiencies of the rest of the cited references. Therefore, because claim 15 incorporates the subject matter of claim 1, and claim 1 is not obvious over the cited art, claim 15 cannot be obvious in light of the cited references either.

D. Claims 18 and 19

The Office rejected claims 18 and 19 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 above, and further in view of EP 0427625 A. As mentioned previously, the Encyclopedia of Controlled Drug Delivery cannot be used to meet the limitation regarding a "plasticizer" recited in the claims because it was published after the filing date of the earliest priority document disclosing that feature. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Claim 18 recites "[a] composition as claimed in claim 11, wherein at least one hair growth-promoting compound is chosen from inner salts of 2,4-diamino-6-alkoxy-3-sulfoxypyrimidine hydroxide having from 1 to 6 carbon atoms in the alkoxy radical, pyridine 1-oxide compounds, and 2,6-diamino-1,3,5-triazine compounds." Claim 19 recites "[a] composition as claimed in claim 18, wherein at least one hair growth-

promoting compound is an inner salt of 2,4-diamino-6-butoxy-3-sulfoxypyrimidine hydroxide." The Office acknowledges that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide. The Office argues, however, that EP 0427625 A "teaches internal salts of 2,4-diamino-6-alkoxy-3-sulfoxypyridimine hydroxide for combating hair loss and inducing/stimulating hair growth." Office Action at 6. The Office further argues that it would have been obvious to one of ordinary skill in the art to add the 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because EP 0427625 A and the rest of the references are all directed toward combating hair loss.

Applicants continue to respectfully traverse this rejection. Claims 18 and 19 depend from claim 1, which would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer, as explained above. EP 0427625 A was cited only for its disclosure of 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide and fails to cure the deficiencies of the rest of the cited references. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

E. Claims 18 and 20

The Office rejected claims 18 and 20 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 92/21317. As mentioned previously, the Encyclopedia of Controlled Drug Delivery cannot be used to meet the limitation regarding a "plasticizer" recited in the claims because it was published after the filing date of the earliest priority document disclosing that feature. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Claim 20 recites "[a] composition as claimed in claim 18, wherein at least one pyridine 1-oxide compound is 2,6-diamino-4-piperidinopyridine." The Office acknowledges that *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery fail to teach 2,4-diamino-4-piperidinopyridine 1-oxide. The Office argues, however, that WO 92/21317 teaches compositions containing a pyridine 1-oxide for combating hair loss and inducing/stimulating hair growth. Office Action at 7. The Office further argues that the reference specifically discloses 2,4-diamino-4-piperidinopyridine 1-oxide. The Office argues that it would have been obvious to one of ordinary skill in the art to add the 2,4-diamino-4-piperidinopyridine 1-oxide to the composition of the combined references because WO 92/21317 and the references are all directed toward combating hair loss.

Applicants continue to respectfully traverse this rejection. Claims 18 and 19 depend from claim 1, which would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a

plasticizer, as explained above. WO 92/21317 was cited only for its disclosure of pyridine 1-oxide compounds and fails to cure the deficiencies of the rest of the cited references. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

F. Claims 18 and 21

The Office rejected claims 18 and 21 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 91/19701. As mentioned previously, the Encyclopedia of Controlled Drug Delivery cannot be used to meet the limitation regarding a "plasticizer" recited in the claims because it was published after the filing date of the earliest priority document disclosing that feature. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Claim 21 recites "[a] composition as claimed in claim 18, wherein at least one pyridine 1-oxide compound is 2,6-diamino-4-piperidinopyridine." The Office admits that the combined references fail to teach 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide. The Office argues, however, that WO 91/19701 teaches compositions containing 2, 6-diamino-1,3,5-triazine derivatives for combating hair loss and inducing/stimulating hair

growth and that 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide is disclosed in the examples. Office Action at 8.

The Office argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made to add 2,6-diamino-4-butoxy-1,3,5-triazine 1-oxide to the composition of the combined references because all of the references are directed toward combating hair loss.

Applicants respectfully traverse this rejection. Claims 18 and 19 depend from claim 1, which as explained *supra*, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. WO 91/19701 was cited only for its disclosure of 2, 6-diamino-1,3,5-triazine derivatives and fails to cure the deficiencies of the rest of the cited references. Therefore, because claims 18 and 19 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

G. Claims 5 and 6

The Office rejected claims 5 and 6 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly*, *Partain*, and the Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 as above, and further in view of Cremophor RH 40 Technical Information, 1997 ("Cremophor pamphlet"). As mentioned previously, the Encyclopedia of Controlled Drug Delivery is

not proper prior art to these claims. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

Claim 5 recites "[a] composition as claimed in claim 1, wherein the at least one plasticizer is chosen from ethoxylated compounds, panthenol, esters of adipic acid, and esters of sebacic acid," and claim 6 recites "[a] composition as claimed in claim 5, wherein the at least one plasticizer is chosen from polyoxyethylated castor oil, ethoxylated cholesterol, and panthenol." The Office admits that the combined references fail to teach polyoxyethylene hydrogenated castor oil. The Office argues, however, that the Cremophor pamphlet teaches that "POE hydrogenated castor oil is skin compatible and solubilizes hydrophobic pharmaceuticals including vitamin A (retinoic acid)." Office Action at p. 9.

The Office argues that it would have been obvious to one of ordinary skill in the art "to modify the composition of the combined references by adding to the composition POE hydrogenated castor oil as motivated by [the Cremophor pamphlet] because (a) Gaillard, Partain, and [the Cremophor pamphlet]all teach using retinoic acid; and (b) [the Cremophor pamphlet] teaches that POE hydrogenated castor oil is a well known solubilizer in pharmaceutical/cosmetic art, which solubilizes hydrophobic pharmaceutical agents to form a clear solution." *Id.*

Applicants respectfully traverse this rejection. Claims 5 and 6 depend from claim 1, which as explained *supra*, would not have been obvious in light of the cited references at least because the combined references fail to teach a composition comprising a plasticizer. The Cremophor pamphlet was cited only for its disclosure of POE hydrogenated castor oil and fails to cure the deficiencies of the rest of the cited

references. Therefore, because claims 5 and 6 incorporate the subject matter of claim 1, and claim 1 is not obvious over the cited references, claims 18 and 19 cannot be obvious in light of the cited references either.

For the foregoing reasons, the Office has not proved a *prima facie* case of obviousness in this rejection and Applicants respectfully request that the rejection be withdrawn.

H. Claims 1, 2, 4, 7, 10-13, 22, 23, 28, 29, 39 and 40

The Office rejected claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 under 35 U.S.C. 103(a) as allegedly being unpatentable over *Gaillard-Kelly* in view of US Patent No. 5,658,559 ("*Smith*") and the Encyclopedia of Controlled Drug Delivery. As mentioned previously, the Encyclopedia of Controlled Drug Delivery is not proper prior art to these claims. For at least this reason, Applicants respectfully request that this rejection be withdrawn.

The Office argues that *Smith* teaches a film-forming lotion composition that forms a barrier on the surface of the skin to prevent evaporative loss of moisture from the skin. The Office further argues that *Smith* teaches polyvinylpyrrolidone/eicosene copolymers, polyvinylpyrrolidone/vinyl acetate copolymers, and polyvinylpyrrolidone/hexadecane copolymers as barrier polymers and polysaccharide polymers for time-controlled release of therapeutic agents. The Office states that *Smith's* therapeutic agents include antiacne compounds and that *Smith's* composition "comprises water and polyhydric alcohols such as propylene glycol and glycerol (plasticizer and solvent)." Office Action at 10.

The Office concludes that it would have been obvious to one of ordinary skill in the art to modify the teachings of *Gaillard-Kelly* by formulating a topical composition comprising the compound of instant formula (I) in the film-forming lotion of *Smith* "because (a) both references are directed to acne treatment compositions; and (b) Smith teaches that the film-forming formulation provides controlled-release of the actives while protecting the skin and prevent loss of moisture of the skin. The skilled artisan would have had a reasonable expectation of successfully producing a stable and effective film-forming lotion which is useful for treating acne or alopecia." *Id.* at 10-11.

1. The combined references fail to teach a composition comprising a plasticizer as instantly claimed

Applicants respectfully traverse this rejection. The issue here is again whether, even if present in the composition, glycerin would meet the limitation of "at least one plasticizer" recited in the instant claims.

As explained *supra*, glycerin is *not always* a plasticizer, and *Smith*, like *Partain*, is completely silent regarding the presence of a plasticizer in its compositions. Because glycerin is not always a plasticizer, then the presence of a plasticizer does not necessarily flow from the combination of references and the Office has failed to show why glycerin would behave as a plasticizer in the compositions of *Smith*. Applicants incorporate herein by reference Applicants' statements made above regarding glycerin having different uses in pharmaceutical compositions, such as a solvent and a humectant.

For at least the foregoing reasons, the combination of references does not render obvious the instant invention and Applicants respectfully request that this rejection be withdrawn.

III. Conclusions

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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By: _____
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Enclosures: a) *Modern Pharmaceutics*, third edition, published by Marcel Dekker, Inc., New York, NY, 1996, pp. 461 and 460.
b) *Remington: The Science and Practice of Pharmacy*, 20th edition, Lippincott Williams & Wilkins, Baltimore, MD and Philadelphia, PA, 2000, p. 1039.